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SAMPLE INJECTION SYSTEM

Field of the Invention

[0001] The present invention relates to sample handling and more particularly to a high throughput sample injection system for liquid sample analysis systems such as liquid chromatography.

Description of the Prior Art

[0002] In performing high pressure liquid chromatography, samples are injected into a mobile phase that is supplied to a sample analysis assembly such as a chromatography column and detector. In order to automate the process and to achieve high sample throughput, an automated liquid handler may be used for supplying the samples in a predetermined sequence. In a known sample injection system, each sample is aspirated with a probe from one of an array of sample containers and the aspirated sample is then dispensed from the probe into a remote injection port associated with an injection valve.

[0003] Although this type of known sample injection system has been quite successful, it is limited in throughput capabilities because of the use of a remote injection port that receives samples dispensed from the liquid handler probe. One difficulty is that sample cross contamination or carryover can occur as sequential samples are dispensed by the probe into the injector port. Such carryover decreases the accuracy of the sample analysis and results in loss of injection reproducibility. Although carryover can be reduced by sufficient intra

sample rinsing, this adds to the time required to perform a series of sample injections and increases sample handling times and reduces sample throughput.

[0004] In a typical known system, the injection port into which samples are dispensed by the probe may be located as much as about two feet from certain ones of the liquid sample containers. Another difficulty is the time and the number of discrete operating steps needed for the liquid handler to move the probe into registration with each sample and then move the probe from the sample to the remote injection port. This also increases sample handling times and reduces sample throughput.

Summary of the Invention

[0005] A primary object of the present invention is to provide a sample injection system having high sample throughput capability and increased injection repeatability but with minimal sample cross contamination carryover. Other objects are to provide a sample injection system in which the time and distance required for sample transfer are minimized and to provide a sample injection system that overcomes problems with known injection systems.

[0006] In brief, in accordance with the invention there is provided a sample injection system including a work surface for supporting a plurality of liquid sample containers and including a probe having a vertical axis. A probe drive system includes an X arm extending horizontally in an X direction, a Y arm slideably mounted on the X arm and extending horizontally in a Y direction, and a Z arm slideably mounted on the Y arm and extending vertically in Z direction. A probe holder holds the probe and is slideably mounted on the Z arm. A probe pump provides positive and negative pressure for the probe for sample dispensing and aspiration. The system includes a sample analyzer and a source of pressurized liquid phase. An injector valve is connected to the probe, to the probe pump, to the source of pressurized liquid phase and to the sample analyzer. A conduit connects the probe to the injector valve and the injector valve is mounted on the probe drive system.

Brief Description of the Drawing

[0007] The present invention together with the above and other objects and advantages may best be understood from the following detailed description of the preferred embodiment of the invention illustrated in the drawings, wherein:

[0008] FIG. 1 is an isometric view of an automated liquid handler having a sample injection system constructed in accordance with the present invention;

[0009] FIG. 2 is an exploded isometric view of the injection valve assembly of the sample injection system;

[0010] FIG. 3 is a schematic illustration of the sample injection system with the injection valve in the sample load position; and

[0011] FIG. 4 is a schematic illustration of the sample injection system with the injection valve in the sample injection position

Detailed Description of the Preferred Embodiments

[0012] Having reference now to FIG. 1 of the drawings, there is illustrated an automated liquid handler 10. The liquid handler 10 is provided with a sample injection system generally designated as 12 and constructed in accordance with the principles of the present invention.

[0013] The liquid handler 10 includes a base 14 providing a work surface 16 for locating and supporting an array of many sample containers or receptacles 18 in which liquid samples are held. The containers can take many forms, including microplates, test tubes and bottles. A control housing 20 is located at one end of the base 14. Liquid samples are aspirated from the containers 18 by a hollow probe 22 moved relative to the work surface 14 by a probe drive system 24.

[0014] The probe drive system is a three axis X-Y-Z drive system. An X arm 26 extends horizontally in an X direction and is supported

along the rear of the work surface 16 between the upstanding control housing 20 and a support pedestal 28. A Y arm 30 extends horizontally in a Y direction from the X arm 26. The base of the Y arm 30 is slideably supported on the X arm for movement across the work surface 16 in the X direction. An X motor 32 is coupled to the Y arm and drives it in the X direction.

[0015] A Z arm 34 extends vertically in a Z direction from the Y arm 30. The base of the Z arm is slideably supported on the Y arm for movement in the Y direction across the work surface 16. A Y motor 36 is coupled to the Z arm and drives it in the Y direction. The X and Y motors 32 and 36 are operated by a controller 38 (FIGS. 3 and 4) within the control housing 20 in order to precisely position the probe 22 above any selected sample container 18.

[0016] The probe 22 is carried by a probe holder 40. The probe holder 40 is mounted on the Z arm 34 for vertical sliding movement. A Z motor 42 is coupled to the probe holder 40 and drives it in the vertical Z direction. When the probe 22 is aligned with a selected sample container 18, the Z motor 42 is operated by the controller 38 to lower the probe 22 into or raise the probe 22 upwardly from a liquid sample held in the sample container 18.

[0017] The automated liquid handler 10 may be of the construction disclosed in Gilson U.S. patent 4,422,151, incorporated herein by reference. The disclosure of that patent may be referred to for a description of the liquid handler 10 beyond that needed for an understanding of the present invention.

[0018] A syringe probe pump 44 applies positive or negative pressure to the probe 22 for dispensing or aspirating liquid from or into the probe 22. The pump 44 includes a pump piston 46 moved within a cylinder 48 by a syringe pump motor 49 (FIGS. 3 and 4) located within the control housing 20 and operated by the controller 38. A three way syringe pump valve 50 is connected to the syringe pump 44 and is movable between one position in which the syringe pump 44 is able to communicate through a conduit 52 with the probe 22 and another

position in which the syringe pump 44 communicates through a conduit 54 with a container 56 of dilutant or solvent (FIGS. 3 and 4). A syringe pump valve motor 58 (FIGS. 3 and 4) mounted within the control housing 20 operates the valve 50 between its alternate positions under the control of the controller 38.

[0019] The sample injection system 12 includes an injection valve assembly 60 operated by an injection valve interface control module 62 in turn operated in accordance with operating instructions provided by the controller 38. As seen in FIG. 2, the injection valve assembly 60 includes a valve operating motor 64 and a bearing support body 66 supporting a valve head 68. These components are contained between upper and lower housing sections 70 and 72. An internal mounting flange 73 holds the valve components in the housing.

[0020] In the illustrated sample injection system 12, the valve head 68 includes a six port injection valve 74 having ports 76, 78, 80, 82, 84 and 86 (FIGS. 3 and 4). An external sample loop 87 is connected between injector valve ports 78 and 84. However the principles of the invention can be applied to other injector valve systems, such as four port injector valves having an internal sample loop. Under the control of the controller 38 and valve control 62, the injector valve is operated by a motor 88 between a sample loading position (FIG. 3) and an alternate sample injection position (FIG. 4). One commercially available injection valve suitable for use in the sample injection system 12 is a RHEODYNE™ RV700-100 injection valve sold by Rheodyne, L.P., Rohnert park, California 94927.

[0021] The port 76 is connected to the probe 22 by a conduit 90. A conduit 92 connects port 82 to a source of pressurized mobile phase. In the illustrated system, mobile phase is supplied from a container 94 by a high pressure precision pump 96. One suitable pump is disclosed in Gilson et al. U.S. patent 4,326,837, incorporated herein by reference. The disclosure of that patent may be referred to for a description of the pump 96 beyond that needed for an understanding of the present invention. Port 80 is connected by a conduit 98 to a sample analyzer 100. Analyzers of many types could be used with the sample injection

system 12. In the illustrated system, the analyzer includes a high pressure liquid chromatography (HPLC) column 102 communicating with a detector 104. The detector 104, for example, may be an ion detector, a mass spectrometer or other type.

[0022] In operation of the sample injection system 12, the injection valve 74 is placed by motor 88 into the sample loading position of FIG. 3. The probe drive system 24 positions the probe 22 over a selected sample container 18. The Z drive motor 42 lowers the probe into the selected liquid sample. The syringe pump valve 50 is in the position seen in FIGS. 3 and 4. The syringe pump 44 communicates with the probe 22 through a flow path including valve 50, conduit 52, injection valve port 86, the sample loop 87, injection valve port 76 and conduit 90. The syringe pump motor 49 operates to reduce pressure in the syringe pump 44 and liquid sample is aspirated through the probe 22 and into the sample loop 87. During the sample loading operation, mobile phase travels from the pump 94 through injection valve ports 82 and 80 toward the HPLC column 102.

[0023] The injection valve is then operated by motor 88 to the alternate, sample injection position of FIG. 4. Pressurized mobile phase from the pump 96 and conduit 92 enters injection valve port 82 and forces the liquid sample in sample loop 87 along a flow path including the sample loop 87, the injection valve port 80 and the conduit 98 toward the HPLC column 102. The liquid sample from the sample loop is thus entrained in the liquid phase for analysis in the analyzer 100. During the sample injection operation, the probe 22 is in communication with the syringe pump valve 50 through injection valve ports 76 and 86.

[0024] Prior to the next sample loading operation, the probe 22 and conduit 90 are preferably rinsed to reduce cross sample contamination carryover. The probe 22 can be moved to a rinsing station and rinsed with solvent, and/or the probe may be rinsed with solvent provided by valve 50 and the syringe pump 44 from the dilutant container 56.

[0025] In accordance with the invention, the injection valve 74 is mounted near the probe 22, and the probe 22 and the injection valve 74

are connected directly and continuously by the short conduit 90. The injection valve assembly 60 is attached to the drive system 24, and preferably to the Z arm 34 near the top of the Z arm. In this mounting position, the injector valve 74 is close to the vertical axis of the probe 22. The distance between the probe axis and the injector valve is only a few inches, preferably less than six inches. The conduit 90 is flexible to permit vertical motion of the probe 22. The short separation distance between the probe axis and the injection valve 74 permits the conduit 90 to be only several inches long, and preferably less than twelve inches long.

[0026] Because the probe 22 and injection port 76 are continuously interconnected by the conduit 90, it is not necessary for the probe to aspirate liquid sample from a sample container and then dispense the liquid sample into an injection port at a remote location. It is not necessary for the probe to be driven from a selected sample container to a remote injection port. Sample throughput rates are maximized and sample carryover is minimized. High injection reproducibility is achieved.

[0027] While the present invention has been described with reference to the details of the embodiment of the invention shown in the drawing, these details are not intended to limit the scope of the invention as claimed in the appended claims.